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Form PTO-1449

U.S. Department of Commerce  
Patent and Trademark Office

Atty. Docket No.  
60390-G/JPW/GJG/JBC

Serial No.  
09/728,616

INFORMATION DISCLOSURE CITATION  
(Use several sheets if necessary)

Applicants: Arlind L. Castelhan, et al.

Filing Date  
December 1, 2000

Group


U.S. PATENT DOCUMENTS

Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
(P)	5 2 9 6 4 8 4	3/22/94	Coghlan, M. J. et al. (Exhibit 1);			
	5 4 0 9 9 3 0	4/25/95	Spada, A. P. et al. (Exhibit 2);			
	5 5 1 6 8 9 4	5/14/96	Reppert S. M. (Exhibit 3);			
	5 5 8 0 8 7 0	12/3/96	Barker, A. J. et al. (Exhibit 4);			
	5 6 4 6 1 3 0	7/8/97	Shi, G. H. (Exhibit 5);			
	5 6 8 1 9 4 1	10/28/97	Cook, P. D. et al. (Exhibit 6);			
	5 7 1 0 1 5 8	1/20/98	Myers, M. R. et al. (Exhibit 7);			
	5 7 1 4 4 9 3	2/3/98	Myers, M. R. et al. (Exhibit 8);			
	5 7 2 1 2 3 7	2/24/98	Myers, M. R. et al. (Exhibit 9);			
	5 7 4 7 4 9 8	5/5/98	Schnur, R.C. et al. (Exhibit 10);			
	5 7 8 0 4 5 0	7/14/98	Shade, D. L. (Exhibit 11);			
(P)	5 9 6 2 4 5 8	10/5/99	Lohmann, et al. (Exhibit 12);			

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation
					Yes No
WO 9 4 1 7 0 9 0	8/4/94	PCT (Exhibit 13);			
WO 9 5 1 1 6 8 1	5/4/95	PCT (Exhibit 14);			
WO 9 5 2 0 5 9 7	8/3/95	PCT (Exhibit 15);			

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)


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		Document Number						Date	Country	Class	Subclass	Translation	
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		WO	9	6	1	9	4	7	8	6/27/96	PCT (Exhibit 16);		
		WO	9	7	0	5	1	3	8	2/13/97	PCT (Exhibit 17);		
		WO	9	7	3	3	8	7	9	9/18/97	PCT (Exhibit 18);		
		WO	9	8	0	8	3	8	2	3/5/98	PCT (Exhibit 19);		
		WO	9	8	2	2	4	6	5	5/28/98	PCT (Exhibit 20);		
		WO	9	9	0	6	0	5	3	2/11/99	PCT (Exhibit 21);		
		WO	9	9	0	8	4	6	0	2/18/99	PCT (Exhibit 22);		
		WO	9	9	3	3	8	1	5	7/8/99	PCT (Exhibit 23);		
		WO	9	9	4	2	0	9	3	8/26/99	PCT (Exhibit 24);		
		EP	0	3	2	2	2	4	2	6/28/89	EPO (Exhibit 25);		
		EP	0	7	2	9	7	5	8	4/9/96	EPO (Exhibit 26);		
		JP	9	2	9	1	0	8	9	5/11/99	Japan (Abstract Only) (Exhibit 27);		
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)													
		Blazynski C., (1990) "Discrete Distributions of Adenosine Receptors in Mammalian Retina", Journal of Neurochemistry, 53: 648-655 (Exhibit 28);											
		Braas K.M., et al., (1987) "Endogenous adenosine and adenosine receptors localized to ganglion cells of the retina", Proceedings of the National Academy of Science, 84: 3906-3910 (Exhibit 29);											
		Bradford M. M., (1976) "A Rapid and Sensitive Method for the Quantitation of Microgram Quantities of Protein Utilizing the Principle of Protein-Dye Binding", Anal. Biochem., 72: 248-254 (Exhibit 30);											
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		Document Number	Date	Country	Class	Subclass	Translation Yes No
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)							
(H)		Broach, J. R., et al., (1983) "Vectors for high level, inducible expression of cloned genes in yeast", in <u>Experimental Manipulation of Gene Expression</u> . M. Inouye (ed), Academic Press, New York, 83-117 (Exhibit 31);					
		Chen, Y. L., et al., (1997) "Synthesis and Oral Efficacy of a 4-(Butylethylamino)pyrrolo[2,3-d]pyrimidine: A Centrally Active Corticotropin-Releasing Factor <sub>1</sub> Receptor Antagonist", <u>J. Med. Chem.</u> , 40: 1749-1754, (Exhibit 32);					
		Cheng, Y. and Prusoff, W. H. (1973) "Relationship Between The Inhibition Constant ( $K_i$ ) And The Concentration Of Inhibitor Which Causes 50 Per Cent Inhibition ( $I_{50}$ ) Of An Enzymatic Reaction", <u>Biochem. Pharmacol.</u> , 22: 3099-3109 (Exhibit 33);					
		Christianson, T. W. et al., (1992) "Multifunctional yeast high-copy-number shuttle vectors", <u>Gene</u> , 110: 119-122 (Exhibit 34);					
(D)		Duzic, E. et al., (1992) "Factors Determining the Specificity of Signal Transduction by Guanine Nucleotide-binding Protein-coupled Receptors", <u>J. Biol. Chem.</u> , 267: 9844-9851 (Exhibit 35);					
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						Yes	No

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

(6)	Feoktistove, I. et al., (1998) "Adenosine A <sub>2B</sub> receptors: a novel therapeutic target in asthma?", <u>TIPS</u> 19: 148-153 (Exhibit 36);
	<del>GenBank accession numbers S45235 and S56143 (Exhibit 37);</del>
	<del>GenBank accession # S46950 (Exhibit 38);</del>
(12)	Kang, Y. et al., (1990) "Effects of Expression of Mammalian G $\alpha$ and Hybrid Mammalian-Yeast G $\alpha$ Proteins on the Yeast Pheromone Response Signal Transduction Pathway", <u>Mol. Cell. Biol.</u> , 10: 2582-2590 (Exhibit 39);
	Muller, C. E. and Stein, B. (1996) "Adenosine Receptor Antagonist: Structure and Potential Therapeutic Applications", <u>Current Pharmaceutical Design</u> , 2: 501-530 (Exhibit 40);
	Muller, C. E. (1997) "A <sub>1</sub> -Adenosine Receptor Antagonists", <u>Exp. Opin. Ther. Patents</u> 7(5): 419-440 (Exhibit 41);
(16)	Muller, C. E., et al., (1997) "Synthesis and Structure-Activity Relationships of 3,7-Dimethyl-1-propargylxanthine Derivatives, A <sub>2A</sub> -Selective Adenosine Receptor Antagonists", <u>J. Med. Chem.</u> , 40: 4396-4405 (Exhibit 42);
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						Yes	No

## OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

(68)	Nyce J. W. and Metzger J.W., (1997) "DNA antisense therapy for asthma in an animal model", <u>Nature</u> , 385: 721-725 (Exhibit 43);
	Pichler, H. et al. (1986) "Synthese of 7-unsubstituiereten 7H-Pyrrolo[2,3-d] pyrimidines", <u>Liebigs Ann. Chemie.</u> , 9: 1485-1505 (Exhibit 44);
	Seela, F., and Lupke, U., (1977) <u>U. Chem. Ber.</u> , 110:1462-1469 (Exhibit 45);
	Strohmeier, G. R. et al., (1995) "The A <sub>2b</sub> Adenosine Receptor Mediates cAMP Responses to Adenosine Receptor Agonists in Human Intestinal Epithelia", <u>J. Bio. Chem.</u> , 270: 2387-2394 (Exhibit 46);
	Williams, E. F. et al., (1994) "Nucleoside transport sites in a cultured human retinal cell line established by SV-40 T antigen gene", <u>Current Eye Research</u> , 13: 109-118 (Exhibit 47);
(u)	Woods, C. L. and Blazynski, C. (1991) "Characterization of Adenosine A <sub>1</sub> -receptor Binding Sites in Bovine Retinal Membranes", <u>Experimental Eye Research</u> , 53: 325-331 (Exhibit 48);

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JP	5 6 3 9 9 1 3	6/17/97	Lidor, R. et al. (Exhibit 50);			
	5 8 3 4 6 0 9	11/10/98	Horne, D. A. et al. (Exhibit 51);			
	5 8 7 7 2 1 8	3/2/99	Herzig, Y. et al. (Exhibit 52);			
	5 8 7 7 2 2 1	3/2/99	Cohen, S. et al. (Exhibit 53);			
	5 8 8 0 1 5 9	3/9/99	Herzig, Y. et al. (Exhibit 54);			
	5 9 1 4 3 4 9	6/22/99	Cohen, S. et al. (Exhibit 55);			
	5 9 9 4 4 0 8	11/30/99	Cohen, S. et al. (Exhibit 56);			
	6 1 0 3 8 9 9	8/15/00	Horne, D. A. et al. (Exhibit 57);			

FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation	
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WO 9 9 6 2 5 1 8	12/9/99	PCT (Exhibit 49);				
WO 9 4 2 4 1 3 6	10/27/94	PCT (Exhibit 58);				
WO 9 5 1 8 6 1 7	7/13/95	PCT (Exhibit 59).				

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)


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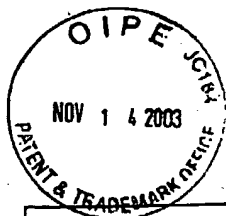
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<i>P</i>		3	0	3	7	9	8	0	6/5/62	Hitchings, G. H. et al. (Exhibit 60);			
FOREIGN PATENT DOCUMENTS													
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		WO	9	3	2	0	0	7	8	10/14/93	PCT (Exhibit 61);		
		WO	9	4	1	3	6	7	6	6/23/94	PCT (Exhibit 62);		
		WO	9	5	1	9	9	7	0	7/27/95	PCT (Exhibit 63);		
		WO	9	8	0	7	7	2	6	2/26/98	PCT (Exhibit 64);		
		WO	9	8	5	7	6	5	1	12/23/98	PCT (Exhibit 65);		
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		EP	0	6	8	2	0	2	7	11/15/95	EPO (Exhibit 67);		
		EP	0	7	2	9	7	5	8	9/4/96	EPO (Exhibit 68);		
		EP	0	7	7	3	0	2	3	5/14/97	EPO (Exhibit 69);		
		GB	9	1	5	3	0	3		1/9/63	GB (Exhibit 70);		
		DE	3	1	4	5	2	8	7	5/19/83	DE (Exhibit 71);		
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)													
<i>P</i>		Iwamura, H. et al. (1996) "Quantitative Aspects of the Receptor Binding of Cytokinin Agonists and Antagonists" J. Med. Chem., 26: 838-844 (Exhibit 72);											
<i>W</i>		Jorgensen, A. et al. (1985) "Synthesis of 7H-Pyrrolo[2,3-d]pyrimidin-4-amines" Liebigs. Ann. Chem., Pages 142-148 (Exhibit 73);											
No Date		Kiichiro, K. et al. "Synthesis of pyrazinecarboxylic acid derivs. - (II) derivs. of 3-aminopyrazinecarboxylic acid" (Abstract only) (Exhibit 74);											
<i>W</i>		Muller, E. C. et al. (1996) "Chiral Pyrrolo[2,3-d]pyrimidine and Pyrimido[4,5,-b]indole Derivatives: Structure-Activity Relationships of Potent, Highly Stereoselective A <sub>1</sub> -Adenosine Receptor Antagonist" J. Med. Chem., 39: 2482-2491 (Exhibit 75);											
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<u>GA</u>	5 6 4 6 1 5 6	7/8/97	Jacobson, et al. (Exhibit 81);			
	5 7 8 0 4 8 1	7/14/98	Jacobson, et al. (Exhibit 82);			
	3 9 1 0 9 1 3	10/7/75	Kim, et al. (Exhibit 83)			

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Document Number	Date	Country	Class	Subclass	Translation
					Yes No
<u>WO</u> 0 0 0 3 7 4 1	1/27/00	PCT (Exhibit 84);			

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<u>GA</u>	Abbracchio M., et al., (1999) "Brain Adenosine Receptors as Targets for Therapeutic Intervention in Neurodegenerative Diseases", <u>Ann. NY. Acad. Sci.</u> , 890: 79-92 (Exhibit 85);
	Abbracchio M., et al., (1997) "Modulation of Apoptosis by Nervous System: a Possible Role for the A <sub>3</sub> Receptor", <u>Ann. NY. Acad. Sci.</u> , 825: 11-22 (Exhibit 86);
	Baraldi P., et al., (2000) "New potent and selective human adenosine A <sub>3</sub> receptor antagonists", <u>Tips</u> , 21: 456-459 (Exhibit 87);
	Brand A., et al., (2001) "Adenosine A1 and A3 receptors mediate inhibition of synaptic transmission in rat cortical neurons", <u>Neuropharmacology</u> , 40: 85-95 (Exhibit 88);
<u>KV</u>	Casavola V., et al., (1998) "Adenosine A3 receptor activation increases cystolic calcium concentration via calcium influx in A6 cells", <u>Drug Development Research</u> , 43 (1): 62 (Exhibit 89)

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Q		Ezeamuzie C., et al., (1999) "Adenosine A3 receptors on human eosinophils mediate inhibition of degranulation and superoxide anion release", <u>British Journal of Pharmacology</u> , 127: 188-194 (Exhibit 90);					
		Fozard J., et al., (1996) "Mast cell degranulation following adenosine A3 receptor activation in rats", <u>European Journal of Pharmacology</u> , 298: 293-297 (Exhibit 91);					
		Franco M., et al., (1999) "Adenosine Regulates Renal Nitric Oxide Production in Hypothyroid Rats", <u>Journal of the American Society of Nephrology</u> , 1681-1688 (Exhibit 92);					
		Guerra L., et al., (1998) "Adenosine A3 receptor activation increases cytosolic calcium influx in A6 cells", <u>Nephrology Dialysis Transplantation</u> , 13 (6): A5 (Exhibit 93);					
Q		Jacobson K.A., et al., (1998) "Adenosine A3 receptors: novel ligands and paradoxical effects", <u>Tips</u> , 19:184-191 (Exhibit 94);					
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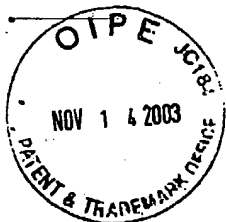


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10		Jacobson K.A., et al., (1997) "Pharmacological Characterization of Novel A3 Adenosine Receptor-selective Antagonists", <u>Neuropharmacology</u> , 36 (9): 1157-1165 (Exhibit 95);					
		Lee T., et al., (2000) "Protective effects of renal ischemic preconditioning and adenosine pretreatment: role of A1 and A3 receptors", <u>Am. J. Physiol. Renal Physiol.</u> , 278: F380-F387 (Exhibit 96);					
		Ohana G., et al., (2001) "Differential Effect of Adenosine on Tumor and Normal Cell Growth: Focus on the A3 Adenosine Receptor", <u>Journal of Cellular Physiology</u> , 186: 19-23 (Exhibit 97);					
		Regulation of Downstream Effectors By GPCRs, (1999) <u>FASEB J.</u> , Abstracts 147.1-147.6 (Exhibit 98);					
		Reshkin J., et al., (2000) "Activation of A3 Adenosine Receptor Induces Calcium Entry and Chloride Secretion in A6 Cells", <u>J. Membrane Biol.</u> , 178: 103-113 (Exhibit 99);					
		Sawynok J., et al., (1997) "Adenosine A3 receptor activation produces nociceptive behaviour and edema by release of histamine and 5-hydroxytryptamine", <u>European Journal of Pharmacology</u> , 333: 1-7 (Exhibit 100);					
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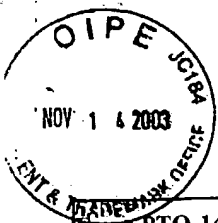
	Von Lubitz, D., et al., (1999) "Chronic administration of adenosine A3 receptor agonist and cerebral ischemia: neuronal and glial effects", <u>European Journal of Pharmacology</u> , 367: 157-163 ( <b>Exhibit 101</b> );
	Von Lubitz D., et al., (1999) "Stimulation of Adenosine A3 Receptors in Cerebral Ischemia", <u>Ann. NY. Acad. Sci.</u> , 890: 93-106 ( <b>Exhibit 102</b> );
	Yao Y., et al., (1997) "Adenosine A3 Receptor Agonists Protect HL-60 and U-937 Cells from Apoptosis Induced by A3 Antagonists", <u>Biochemical And Biophysical Research Communications</u> , 232: 317-322 ( <b>Exhibit 103</b> ); and
	Zhao Z., et al., (2000) "A role for the A3 Adenosine receptor in determining tissue levels of cAMP and blood pressure: studies in knock-out mice", <u>Biochimica et Biophysica Acta</u> , 1500: 280-290 ( <b>Exhibit 104</b> )
	International Search Report for International Application No. PCT/US99/12135 ( <b>Exhibit 105</b> );
	International Search Report for International Application No. PCT/US00/32702 ( <b>Exhibit 106</b> );
	Lee T., et al., (1999) "Protective effects of renal ischemic preconditioning and adenosine pretreatment: role of A1 and A3 receptors", <u>72<sup>nd</sup> Scientific Sessions of the American Heart Association</u> , Atlanta, GA, p.197 ( <b>Exhibit 107</b> );

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Atty. Docket No.  
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Serial No.  
09/728,616

Applicants: Arlind L. Castelhana, et al.

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FOREIGN PATENT DOCUMENTS

	Document Number	Date	Country	Class	Subclass	Translation	
						Yes	No
64	WO 9 8 2 9 3 9 7	7/9/98	PCT (Application with English abstract) (Exhibit 108);				
	WO 9 7 0 2 2 6 6	1/23/97	PCT (Exhibit 109);				
	IN 1 5 7 2 8 0	2/22/86	India (Exhibit 110);				

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

	Mautner, H.G., (1961) "Potential Deoxyribonucleic Acid Cross-linking Agents. 8,8'-Bisporines", J. Org. Chem. 26(6):1914-1917 (Exhibit 111); and
12	PCT International Preliminary Examination Report for International Application No. PCT/US99/12135 (Exhibit 112).

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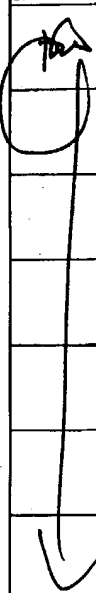

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Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date if Appropriate
	09 4 5 4 0 7 5	12/2/99	Arlindo L. Castelhana, et al. (Exhibit 1);			
	09 4 5 4 0 7 4	12/2/99	Arlindo L. Castelhana, et al. (Exhibit 2);			
	20 02 00 58 6 6 7	5/16/02	Arlindo L. Castelhana, et al. (Exhibit 3);			
	20 03 00 36 5 4 5	2/20/03	Arlindo L. Castelhana, et al. (Exhibit 4);			
	20 02 00 28 7 8 2	3/7/02	Arlindo L. Castelhana, et al. (Exhibit 5);			
	20 03 00 45 5 3 6	3/6/03	Arlindo L. Castelhana, et al. (Exhibit 6);			
	20 03 00 73 7 0 8	4/17/03	Arlindo L. Castelhana, et al. (Exhibit 7);			
	10 0 1 0 0 9 2	11/30/01	Arlindo L. Castelhana, et al. (Exhibit 8);			

## FOREIGN PATENT DOCUMENTS

Document Number	Date	Country	Class	Subclass	Translation
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